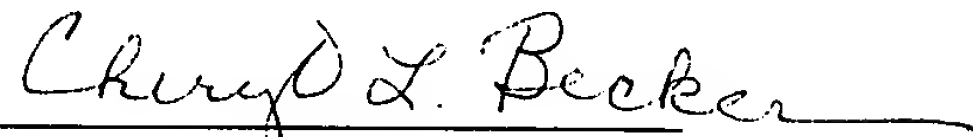


REMARKS

It is respectfully requested that the above amendments to the specification be entered prior to an examination of the case.

Should any questions arise concerning the above, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

Respectfully submitted,



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MARKED UP VERSION OF SPECIFICATION SHOWING CHANGES MADE

Please amend page 22, line 6 - page 24, line 21 as follows:

A plasmid containing nucleotides 14-5294 of the H strain of HCV (N. Ogata, H. Alter, R. Miller, and R. Purcell, *Proc. Natl. Acad. Sci. USA* 88:3392-3396 (1991)) in pGEM-9Zf(-) (Promega Corp., Madison, WI) was partially digested using DNase I by the following method in order to obtain random epitope-encoding fragments. Five µg aliquots of plasmid DNA were incubated at 15°C for 10 minutes in 0.5 M Tris-HCl pH 7.6, 10 mM MnCl₂ in the presence of anywhere from 0.1 to 0.7 units of DNase I. Aliquots from each digestion were analyzed by agarose gel electrophoresis. The two digestion mixtures containing 0.6 and 0.7 units of DNase I were found to give the largest amount of fragments in the 50-200 bp range. These two mixtures were pooled and extracted one time with an equal volume of phenol-chloroform (1:1, v/v) then precipitated by the addition of one tenth volume 3 M sodium acetate and 2.5 volumes 100% ethanol followed by centrifugation at 14,000 x g for 10 minutes. The ends of the DNA molecules were then made blunt using the PCR Polishing kit (Stratagene, Inc., La Jolla, CA) as per manufacturer's directions. The DNA was again extracted and precipitated as described above, followed by ligation to a double-stranded adaptor in a 10 µl reaction volume using a T4 DNA ligase kit (Stratagene, Inc., La Jolla, CA) as directed by the manufacturer. The sequence of this double stranded adaptor was:

5'-GATCGCTCGAATTCCTCG-3' [(SEQUENCE ID NO:1)] SEQUENCE ID NO:17)

3'-TTCTAGCGAGCTTAAGGAGC-5' [(SEQUENCE ID NO:2)] (SEQUENCE ID NO:18)

The sense-strand oligonucleotide of the [adapator] adaptor [(SEQ ID NO:1)] (SEQ ID NO:17) was then used as a primer in a PCR reaction such that all DNAs were amplified independent of their sequence. This method is a modification of that described by A. Akowitz and L. Manuelidis, *Gene* 81:295-306 (1989) and G. Reyes and J. Kim, *Mol. Cell. Probes* 5:473-481 (1991). PCR was performed in the presence of the sense-strand oligonucleotide primer at a final concentration of 1 μ M in a reaction volume of 100 μ l using the GeneAmp Gold PCR kit (PE Applied Biosystems, Foster City, CA) as directed by the manufacturer in a PE-9600 thermocycler. A pre-incubation at 94°C for 8 min was followed by twenty-five cycles of PCR as follows: denaturation at 94°C for 20 seconds, annealing at 55°C for 30 seconds, and extension at 72°C for 1.0 min. This was followed by a final extension step at 72°C for 10 min. The PCR product was extracted and precipitated as described above. The entire PCR was run on a 1.2% agarose gel and a gel slice containing DNA fragments between approximately 70 and 250 bp was removed. The DNA was extracted from the gel slice using the QIAEX II kit (QIAGEN, Inc., Valencia, CA) as per manufacturer's directions. The DNA was digested with the restriction enzyme EcoRI (New England Biolabs, Beverly, MA) as directed by the manufacturer. The digested DNA was then extracted and precipitated as described above.

Please amend page 49, lines 13-25 as follows***:

Table IV shows the mean signal-to-negative (S/N) values obtained upon testing the various pairs of monoclonal antibodies for their ability to detect HCV core antigen in the positive control human plasma (nd: not determined).

From this data, it is apparent that some pairs of [monoclonalantibodies] monoclonal antibodies exhibit greater sensitivity than others and that the sensitivity was dependent upon the proper configuration of the assay. For example, when monoclonal antibody A05 was used as the capture reagent and C11-10 was used as the detection reagent, the resulting S/N value was 150.0, however, when the opposite configuration was used, the resulting S/N value was only 6.8.

***The paragraph was also reformatted so that each line begins at the left margin.